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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,867	12/06/2001	Audrey Goddard	P3230R1C1	6830

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EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

11L

Office Action Summary	Application No.	Applicant(s)	
	10/006,867	EATON ET AL.0	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 42-44, and 51 have been amended and claims 42-51 are pending and under examination.

2. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Rejections Withdrawn

3. The rejection of claims 42-45, 47, 50-51 under 35 U.S.C. 102(a) as being anticipated by Feng et al (WO 99/24836, published 5/99) is withdrawn in view of the 131 declaration filed.

Response to Arguments

4. The rejection of claims 42-51 under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility is maintained.

The response filed 12/13/04 has been carefully considured but is deemed not to be persuasive. The response states that that utility need not be proved to be absolute but a correlation between the evidence and the asserted utility is sufficient and more likely than not a person of skill in the art would be convinced that the asserted utility is true (see pages 5-7 of response) and Applicants have established that the gene encoding the PRO180 polypeptide is differentially expressed in certain tumors compared to normal and the polypeptide is useful as a diagnostic tool (see page 8 of

response). In response to this argument, while a correlation between the evidence and asserted utility may be sufficient this has not been demonstrated in the instant application. The evidence is not correlated because the art is so unpredictable and as such a person skilled in the art would not be convinced that the asserted utility is true. While the data in Example 18 shows the nucleic acid is differentially expressed, there is no data for the polypeptide or any other nucleic acid other than SEQ ID NO:1 being differentially expressed in any tumor. The response states that the Office has not offered any reason to reject the declarations of Grimaldi or Polakis previously submitted (see page 8 of response). In response to this argument, this was addressed in the previous response that the declaration states that we have showed that in 80% of the observations they have found that increased levels of a mRNA correlates with a change in protein levels. In response to this argument, the examiner cited art in the 112 first rejection that supports that mRNA over-expression does not correlate with protein over-expression. While the declaration may show protein over-expression in some cases, the references cited on page 11 of the response, only show mRNA overexpression. Even though the declaration does show some protein correlation, there are equally references that show this not to be the case and these were cited in the rejection such as Chen et al (Molecular and Cellular Proteomics 1:304-313, 2002) underscore the unpredictability in the art as showing that protein expression does not correlate with gene over-expression.

The response states that applicants have established that the accepted understanding in the art is that there is a reasonable correlation between gene

expression and expression of the protein (see page 8 of response) and reiterate statements from the Grimaldi and Polakis declarations which in response to this was addressed above. The response then cites Alberts for teaching correlation between gene expression and increased protein and cites page 302 Figure 6-3 and figure 6-90 and text citing "the initiation of transcription is the most common point for a cell to regulate the expression of each of its genes" at page 364 (see page 9 of response). In response to this argument, while Alberts is a basic molecular biology text and discusses the well known mechanism of protein expression, and that initiation may be the most common regulation, he states "A cell typically expresses only a fraction of its genes" (see page 379) and that the mechanism is complicated as cited on page 435 in the summary where it is stated "in eukaryotes the transcription of a gene is generally controlled by combinations of gene regulatory proteins. Therefore, it appears that Alberts provides support that not all genes would be expressed into protein and that there are numerous controls as cited by the examiner in the Genes VI paper.

The response then discusses the art of Zhigang et al with regard to expression of PSCA protein and mRNA and the correlation of each (see pages 9-10 of response). In response to this argument, again although applicants have supplied some references to show in some cases mRNA correlates with protein expression, the examiner has cited numerous articles that show this not to be the case and therefor, the art is unpredictable.

The response then addresses the Chen reference in the previous Office action cited by the examiner. The response states that while it is true that there is no

necessary correlation between protein and gene expression because of other mechanisms for regulation of gene expression, the article recognizes the role of both mRNA and protein in the diagnosis of cancer (see page 10 of response). In response to this it appears that applicants are stating that there is no clear correlation between gene expression and protein expression and it is true that genes as well as proteins can be used for diagnostics.

The response then addresses the Genes VI paper and states that it is the transcription of the gene that is most influenced in the control sep (see page 11 of response). In response to this argument, again the reference teaches production of RNA can not inevitably be equated with protein production. while the translation of the gene may be the majority of the regulation the art teaches that there are numerous regulatory elements for the production of the protein. Just because the gene is transcribed does not predict protein translation.

The references cited by the examiner demonstrate that there is no clear "reasonable" correlation between gene expression and protein production and even though applicant has provided references showing in some specific instances that there is a correlation between gene and protein production, there is an equal number of instances that show this not to be the case and therefore it is unpredictable whether the protein would be produced and therefore, the utility is not substantial.

5. The rejection of claims 42-51 under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well

established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention is maintained for the reasons above.

6. The rejection of claims 42-43, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 12/13/04 has been carefully considered but is deemed not to be persuasive. The response states that the current invention is adequately described and according to the teachings of the specification based on the cloning and expression of variants of PRO 180 the description of the gene expression assay and reduction of practice of SEQ ID NO:1 and 2 and the functional recitation in the claims the applicants were in possession of the subject matter (see page 13-14 of response). In response to this argument, applicants do not describe any polypeptide having 95 or 99% identity to SEQID NO:2 or its extracellular domain which is over expressed in rectal tumors or normal lung. Just because one teaches how one could potentially obtain such a molecule does not give one possession of the molecule. There is no indication that such a molecule exists or what the structure of the molecule would be based on the detailed description of the cloning and expression of variants of PRO180 in the specification. Only SEQ ID NO:1 is amplified in tumors which encodes SEQ ID NO:2 and there is no polypeptide that is overexpressed in rectal tumors. Describing assays to find the polypeptide does not describe such polypeptides. The specification does not

describe any other nucleic acid that encodes any polypeptide that is 95-99% identical to SEQ ID NO:2 which is encoded by a nucleic acid that is over-expressed in rectal tumors.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class.

7. The rejection of claims 42-43, 50-51 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

The response filed 12/13/04 has been carefully considered but is deemed not to be persuasive. The response seems to combine this rejection with the above written description and states that the invention relates to recombinant DNA technology and the persons in the art are at a high level of skill and the specification teaches assays and gene expression assays (see page 14 of response). In response to this argument, the specification does not describe how to make polypeptides that are 95-99% identical to SEQ ID NO:2 wherein the nucleic acid is overexpressed. The specification does not teach a screen or other such molecules. In addition the arguments presented does not overcome the utility rejection. Therefore one would not know how to make or use such molecules.

Conclusion

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached at (571) 272-0787.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is 571-373-8300.

Larry R. Helms

571-272-0832

LARRY R. HELMS, PH.D
PRIMARY EXAMINER